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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,665	01/09/2002	Thomas Schupp	4-21001B/C1	7007
1095	7590	07/06/2004	EXAMINER	
NOVARTIS CORPORATE INTELLECTUAL PROPERTY ONE HEALTH PLAZA 430/2 EAST HANOVER, NJ 07936-1080			VOGEL, NANCY S	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 07/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/042,665	Applicant(s) SCHUPP ET AL.	
	Examiner Nancy T. Vogel	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-30 is/are pending in the application.
 4a) Of the above claim(s) 15-18 and 27-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 19-26 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>4/11/02</u> . | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

Claims 15-30 are pending in the case.

Election/Restrictions

Applicant's election of Group I, and the species ORF A, in the reply filed on 4/8/04 and in a phone conversation on or about 6/1/04 with attorney John Prince is acknowledged. Because applicant did not distinctly and specifically point out errors in the restriction requirement, or state that the election was traversed, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 15-18, and 27-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/08/04.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 22 and 24-26 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims read on naturally occurring, non-isolated DNA fragments. The claims read on products of nature, and fail to show the "hand of man". Amendment to include the phrase "An isolated DNA fragment..." would be remedial.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 22 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Donadio et al. (Science 252-675-679 (1991)).

Donadio et al. disclose a DNA fragment comprising at least 15 consecutive nucleotides which are the same as 15 consecutive nucleotides from SEQ ID NO: 3 of the instant application (see sequence alignment of sequence disclosed in reference, compared to a 15-mer from SEQ ID NO:3 of instant application, attached).

Claims 22 and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Brown et al. (US Patent 5,763,569).

Brown et al. disclose a DNA fragment comprising at least 15 consecutive nucleotides which are the same as 15 consecutive nucleotides from SEQ ID NO: 3 of

the instant application (see sequence alignment of SEQ ID NO:1 of reference, compared to a 15-mer from SEQ ID NO:3 of instant application, attached).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims 25 and 26 are drawn to a DNA fragment according to claim 25, wherein said fragment comprises a nucleotide sequence selected from the group consisting of ORF A, B, C, D, E and functional fragments thereof, or encoding one or more proteins or polypeptides, or functional derivatives thereof, depicted in SEQ ID NOS 4 to 9.

The specification discloses SEQ ID NO: 1, and SEQ ID NO:3 which corresponds to the cDNA and the DNA encoding the polypeptides depicted in SEQ ID NOS 4-9. However, claims 25 and 26 are drawn to a DNA fragment from the genome of *Amycolaptosis mediterranei*, and the fragment comprises a nucleotide sequence selected from the group consisting of ORF A, B, C, D, E and F, or functional fragments

thereof, or a nucleotide sequence encoding one or more of the polypeptides depicted in SEQ ID NOs 4-9, or functional derivatives thereof. The functional fragments and derivatives thereof do not meet the written description provision of 35 U.S.C. 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

With the exception of ORF A, B, C, D E, and F of SEQ ID NO 3, or polynucleotides encoding SEQ ID NO: 4-9, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides or polypeptides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid or polypeptide itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. And in University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405, held that:

... To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he

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description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.”). Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the polynucleotides which are ORF A, B, C, D, E, or F of SEQ ID NO: 3, or polypeptides of SEQ ID NO: 4-9 but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. (see page 1115).

Claims 19-22 and 24-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotides whose sequence is shown in ORF A, or the other ORF's of SEQ ID NO: 3, does not reasonably provide enablement for functional fragments thereof which have at least 15 consecutive nucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention. The invention claimed is a DNA fragment from the genome of *Amycolatopsis mediterranei* which is involved in the gene cluster responsible for rifamycin synthesis, which is SEQ ID NO 1 or SEQ ID NO 3 or at least 15 consecutive nucleotides therefrom.

The state of the prior art. The state of the prior art regarding prediction of function and activity of any particular polypeptide in a biosynthetic process such as rifamycin biosynthesis, is not advanced. Despite considerable advances in elucidation of genes and the proteins encoded by said genes in such biosynthetic processes, it is still not possible to predict which fragments will result in a functional protein.

The presence of working examples. The specification does not contain any working examples of fragments of the disclosed ORF polynucleotides or the proteins they encode, which retain function or role in rifamycin biosynthesis.

The level of predictability in the art. There is no predictability that any deletion, modification, or derivative of the disclosed complete gene sequences shown in SEQ ID NO: 3 would maintain function or involvement in rifamycin biosynthesis.

The amount of guidance by the inventor. The specification does not give guidance or methods to determine which 15 consecutive nucleotides of the DNA fragments would be functional and are involved in the gene cluster responsible for rifamycin synthesis. The specification does not have sufficient guidance for choosing which of the 15 consecutive nucleotides of the recited DNA fragments would be considered to have function in rifamycin biosynthesis. The specification does not have guidance regarding which 15 consecutive nucleotides to select which has a function in polyketide synthase in rifamycin synthesis.

In view of the state of the prior art, the lack of working examples, the unpredictability of the art, and the lack of guidance in the specification, it would require undue experimentation to practice the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-26 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19-23 are vague and indefinite in their dependence, either directly or indirectly, on cancelled claim 1. In the interest of compact prosecution, it has been assumed that claims 19, 20, and 22 recite "claim 24" instead of "claim 1".

Claim 23 provides for the use of the hybridization probe of claim 22, but, since the claim does not set forth any steps involved in the method/process, it is unclear what

method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.


Claim 23 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 24 is vague and indefinite in its recitation of “the DNA region involved in the gene cluster...”. It is not clear what is intended by the term “involved” in this claim, and therefore the intended metes and bounds cannot be determined. It is not clear how a DNA region is “involved” in a gene cluster. It is also unclear in its recitation of “by reason of its function in connection with rifamycin biosynthesis”, since it is not clear what the recited “function in connection” is intended to mean. The claim is additionally vague and indefinite in the recitation of “which is SEQ ID NO 1 or SEQ ID NO 3...”. It is not clear what “which” is referring to.

Claim 25 is vague and indefinite in its recitation of “said fragment comprises a nucleotide sequence selected from the group consisting of ORF A, B, C, D, E, F, and functional fragments thereof, or encodes one or more of the proteins or polypeptides, or functional derivatives thereof...”. It is not clear which fragments and which derivatives are being referred to, and therefore the intended metes and bounds cannot be determined. Clarification is required.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

6/21/04


TERRY MCKELVEY
PRIMARY EXAMINER

Claim 26 is vague and indefinite in its recitation of "A DNA fragment... wherein said fragment comprises a nucleotide sequence which is ORF A, or functional derivatives thereof, depicted in SEQ ID NO 4". The molecule depicted in SEQ ID NO 4 is the polypeptide that is encoded by ORF A of the SEQ ID NO 3 sequence, defined in the specification as nucleotide numbers 1825-15543 of SEQ ID NO 3. Presumably this is what is intended in the claim and in the interest of compact prosecution, the claim has been examined as if this were recited. Clarification is required.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.